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SHORT COMMUNICATION

Cutaneous B-cell Pseudolymphoma in a Psoriatic Patient Treated with Cyclosporine

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Cyclosporine (Cys) is used as an oral therapy for psoriatic patients with moderate to severe eruptions (1). Pseudolymphoma has been reported in psoriatic patients treated with Cys (2), infliximab (3, 4) or adalimumab (4). Cys is an immunosuppressant that acts via binding to the T-cell cytosolic protein, cyclophilin, and several cases of Cys-related T-cell pseudolymphoma have been reported (3, 5). We report here a psoriatic patient who received long-term Cys treatment and developed B-cell pseudolymphoma on his face and ear. After discontinuing Cys treatment, the eruptions rapidly disappeared and did not recur during 18 months of follow-up.

CASE REPORT

A 65-year-old Japanese man with psoriasis vulgaris was treated over a 20-year period with Cys (2.0–3.0 mg/kg/day), but no other systemic immunosuppressive drugs, at a private dermatology clinic. He noticed the development of an erythematous nodule on his nose, followed by a rapid increase in the number of eruptions on his nose and cheeks. Thus, he visited our department 3 months after the onset of the eruptions. On the first consultation, multiple red, dome-shaped nodules (5–20 mm in size) were observed on his nose, forehead, chin, cheeks and right ear (Fig. 1a). The lesions were neither painful nor itchy. The patient had no other skin eruptions or lymph node swelling. Laboratory data were within normal limits, except for a slight elevation in serum soluble interleukin-2 receptor level (588 U/ml). Similarly, computed tomography images of the chest and abdomen did not reveal any abnormal findings.

The pathological examination of a skin biopsy specimen from an erythematous nodule on the patient's chin showed nodular dermal infiltration by lymphoid cells, and formation of germinal centres. Dense cell infiltration was evident from the papillary to reticular dermis, with a "top-heavy" distribution. Lymphoid cell infiltration into the epidermis was absent, but a "Grenz zone" was present (Fig. 1b, 1c). These cells formed follicular structures, and some disrupted lymphocytes were apparent within the follicle. The lymphoid cell infiltration extended to areas around the hair follicle appendage, without disrupting the hair follicle. Furthermore, immunostaining showed that the cells forming the follicular structures were positive for CD20, CD79a and bcl-6,

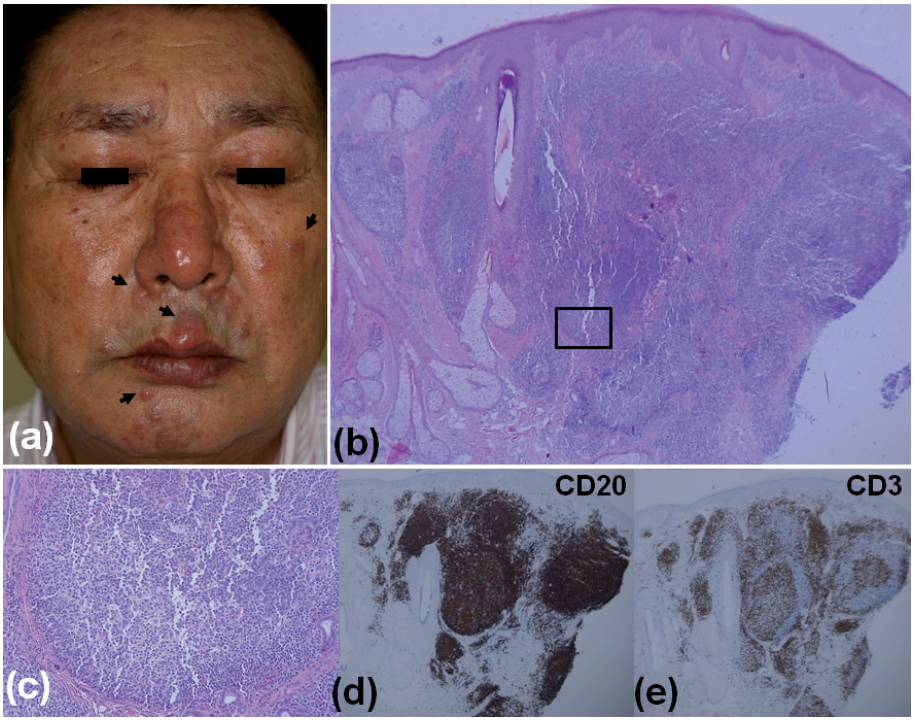

Fig. 1. (a) Clinical findings on the patient's face on the initial consultation, showing multiple red, dome-shaped nodules (*arrows*). Histological findings by haematoxylin and eosin staining, at (b) original magnification ×40 and (c) original magnification ×200; and immunostaining for: (d) CD20 (original magnification ×400) and (e) CD3 (original magnification ×400). A written permission from the patient is given to publish this photo.

but negative for MUM-1; some of these cells were also bcl-2-positive (Fig. 1d, 1e). CD3-positive T cells were observed around the follicles and, in some areas, within the follicle. All of the infiltrating cells were negative for Epstein-Barr virus-encoded RNA. Gene rearrangement analysis was not performed. Based on these clinical and histopathological findings, a diagnosis of B-cell pseudolymphoma was made, probably caused by Cys. Following diagnosis, the patient discontinued oral Cys treatment. As a result, his skin lesions had mostly disappeared within 1 month, and were completely absent within 5 months. Pseudolymphoma did not recur during the 18-month follow-up and recurrent psoriatic lesions were treated with topical steroids and vitamin D3.

DISCUSSION

Pseudolymphomas are classified into either B-cell- or T-cell-type. B-cell pseudolymphoma is sometimes difficult to distinguish from true B-cell lymphoma, particularly marginal zone lymphoma and follicle centre lymphoma. The important pathological findings for the B-cell pseudolymphoma include: (*i*) a well-defined, "top-heavy" infiltrate of lymphocytes into the upper dermis, (*ii*) lack of epidermal lymphoid cells infiltration, (*iii*) a Grenz zone, (*iv*) germinal centre formation, (*v*) lymphocyte nuclear fragments (tingible bodies) and macrophages with cytoplasmic tingible bodies, and (*vi*) infiltrates of histiocytes, eosinophils, and plasma cells around germinal centres (6). Previously, a case of cutaneous B-cell pseudolymphoma was reported to have eventually progressed to cutaneous B-cell lymphoma (7); therefore, the potential for conversion to malignancy requires attention. However, uncertainty remains regarding whether the patients with malignant conversion initially had lymphomas that were histologically misdiagnosed or whether they initially harboured lymphocyte clones as an early step in a multistep progression pathway to cutaneous lymphoma (6). Lymphocytic infiltrate of the skin (pseudolymphoma), involving mainly T cells, has been reported following Cys treatment (5). Pseudolymphoma has also been described in association with tattoos, vaccinations, infections, drugs and inflammatory dermatoses, even though most cases are idiopathic (8). Drug-induced cutaneous pseudolymphoma is most commonly reported in conjunction with the use of anti-epileptic agents, but some cases have been reported to occur in association with Cys treatment (2). In our patient, the rapid disappearance of the pseudolymphoma eruptions after Cys discontinuation, and their lack of recurrence, strongly suggested a causal relationship between Cys use and the onset of pseudolymphoma. In a prospective 5-year study of 1,252 patients with psoriasis who were treated with Cys for a mean of 1.9 years, malignancies were reported in 47 patients (3.8%), including 3 with leukaemia and 2 with lymphoma (9). However, the incidence of non-skin malignancies was not significantly higher in this study.

The risk of lymphoproliferative malignancies associated with Cys use in psoriatic patients remains poorly defined. However, the majority of these adverse effects are related to dose and treatment duration (2). To avoid the risk of adverse effects, including malignancy, short-term administration of Cys (8) and intermittent short (mean 12 weeks) courses of Cys (10) are preferred. In our patient, long-term treatment with Cys, albeit at a low dose, is a possible cause of the onset of pseudolymphoma.

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